Claims (clean version encompassing amendments)

1. A method of imaging of an animate human or non-human animal body, which method comprises: administering parenterally to said body a particulate material comprising a matrix or membrane material and at least one contrast generating species, which matrix or membrane material is responsive to a pre-selected physiological parameter whereby to alter the contrast efficacy of said species in response to a change in the value of said parameter; generating image data of at least part of said body in which said species is present; and generating therefrom a signal indicative of the value or variation of said parameter in said part of said body.

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2. (once amended) A method as claimed in claim 1 wherein the physiological parameter is pH, temperature, pressure, carbon dioxide tension, enzyme activity, tissue electrical activity, tissue water diffusion or ion concentration.

3. A method as claimed in claim 2 wherein the physiological parameter is pH, temperature or pressure.

4. (once amended) A method as claimed in claim 1 wherein the response of the matrix or membrane material to a change in the value of the pre-selected physiological parameter is a change in matrix or membrane permeability or chemical or physical breakdown of the matrix or membrane material.

5. (once amended) A method as claimed in claim 1 wherein the imaging technique is MRI, scintigraphy or ultrasound or X-ray imaging.

6. (once amended) A method of MRI as claimed in claim 5 wherein the contrast generating species is selected from a group consisting of a paramagnetic compound, a superparamagnetic compound, an iron oxide, a gadolinium compound and a dysprosium compound.

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9. A method as claimed in claim 1 wherein said particulate material is in combination with a targeting ligand for a cell or receptor of interest.

10. (once amended) A method as claimed in claim 1 wherein the matrix or membrane material forms a vesicle.

11. A method as claimed in claim 1 wherein the matrix or membrane material is selected from a phospholipid and a physiologically acceptable polymer.

12. (twice amended) A method as claimed in claim 10 wherein the matrix or membrane material forms a temperature or pH sensitive liposome.

13. A method as claimed in claim 12 wherein the liposome is stable at normal body temperature but exhibits increased water permeability or leakage at temperatures greater than normal body temperature.

23. A method of imaging of an animate human or non-human animal body, which method comprises:

administering parenterally to said body at least one contrast generating species the contrast efficacy whereof is responsive to a change in value of a pre-selected physiological parameter;

generating image data of at least part of said body in which said species is present; and

generating therefrom a signal indicative of the value or variation of said parameter in said part of said body and also generating an anatomical image of the same part of the animal body.

24. Method as claimed in claim 10 wherein the matrix or membrane material is responsive to temperature and the change in the value of temperature results from external heating.

25. A method as claimed in claim 24 wherein said external heating is carried out using focused ultrasound.

26. A method as claimed in claim 24 wherein the matrix or membrane material

comprises a lipid or a lipid mixture having a Tc value between 35 and 80°C.

27. A method as claimed in claim 25 wherein the matrix or membrane material comprises a lipid or a lipid mixture having a Tc value between 35 and 80°C.

28. A method as claimed in claim 26 wherein the change in the value of said parameter results from external heating, the external heating being carried out using focused ultrasound.

29. A method as claimed in claim 27 wherein the change in the value of said parameter results from external heating, the external heating being carried out using focused ultrasound.

30. A method as claimed in claim 1 wherein the contrast efficacy is altered by interaction between the contrast generating species and the environment in the part of the animate human or non-human animal body where the matrix or membrane material has responded to a change in the value of the physiological parameter.

31. A method as claimed in claim 1 wherein the physiological parameter is temperature and wherein the change in the value of said parameter is related to cancer, cardiovascular disease or inflammation or results from external heating in the animate human or non-human animal body.

32. A method as claimed in claim 28 wherein the physiological parameter is pH and wherein the change in the value of said parameter is caused by cancer, cardiovascular disease, osteoporosis, inflammations or autoimmune diseases.

33. A method as claimed in claim 32 wherein in addition to the generation of a signal indicative of the value or variation of a pre-determined physiological parameter in a part of the animate human or non-human animal body in which the contrast generating species is present, an anatomical image of the same part of the animate human or non-human animal body is generated.

34. A method as claimed in claim 33 wherein no contrast agent is used to generate the anatomical image.

35. A method as claimed in claim 33 wherein a contrast agent is used in the generation of the anatomical image.

36. A method as claimed in claim 30 wherein the same contrast agent is used to generate a signal relating to the pre-selected physiological parameter and the anatomical image.

37. A contrast medium for imaging of a physiological parameter, said medium

comprising a particulate material the particles whereof comprise a matrix or membrane material and at least one contrast generating species, said matrix or membrane material being responsive to a physiological parameter to cause the contrast efficacy of said contrast generating species to vary in response to said parameter.

38. A method of imaging of an animate human or non-human animal body, which method comprises:

administering parenterally to said body at least one contrast generating species the contrast efficacy whereof is responsive to a change in value of a pre-selected physiological parameter;

generating image data of at least part of said body in which said species is present; and

generating therefrom a signal indicative of the value or variation of said parameter in said part of said body and also generating an anatomical image of the same part of the animal body.

Specification (marked up copy showing amendments)

The paragraph on page 16, lines 8-24:

The physiological parameter studied using the method of the invention may be any physiochemical parameter capable of affecting the matrix or membrane material of the contrast agent, e.g. pressure, temperature, pH, oxygen tension, carbon dioxide tension, enzyme activity, metabolite concentration, tissue electrical activity, tissue water diffusion, ion concentration, particularly Mg^{2+}, Ca^{2+} and Zn^{2+}, etc. Preferably however it will be selected from blood parameters, e.g. pressure, temperature and pH, in particular in the vasculature rather than the chambers of the heart. Where temperature is being measured, changes may be due to intrinsic factors such as disease or because of external factors, i.e. hyperthermia. It is not envisaged that the parameter be one which does not affect the membrane or matrix, for example flow rate or perfusion density.